Technical Comments

Epilepsy Hypothesis

The report "Decreased hippocampal inhibition and a selective loss of interneurons in experimental epilepsy" by Robert S. Sloviter (*1*) demonstrates a loss of somatostatin-containing hilar neurons ipsilateral to perforant path stimulation. However, the report contains incomplete immunocytochemical results for γ-aminobutyric acid (GABA) neurons in the hilus of the dentate gyrus. The author does not appear to have replicated the findings of many investigators (*2–4*) who have shown large numbers of GABAergic hilar neurons. In fact, two of these studies (*3*) have shown that many somatostatin-containing neurons in the hilus are GABAergic. This finding was expected because many GABAergic hilar neurons resemble the morphology of somatostatin neurons in the hilus of the rat, and it is now clear that both GABAergic (*4*) and somatostatin-containing hilar neurons in the rat have commissural and associational projections. Therefore, the loss of somatostatin hilar neurons indicates that significant numbers of GABAergic hilar neurons are also degenerating.

It is possible that Sloviter's immunocytochemical results for GABAergic neurons in the hilus are related to the fixation protocol, in which a low concentration of glutaraldehyde (0.01%) was used. Although this fixative provides good staining for peptide-containing neurons, the antiserum to GABA is usually more effective with preparations that are fixed with higher concentrations of glutaraldehyde (*2, 3*). In order to use these same preparations to localize GABAergic neurons, it might be better to use an antiserum to glutamate decarboxylase (the synthesizing enzyme for GABA) that does not require glutaraldehyde in the fixative.

Sloviter interprets his results as indicating that GABAergic hilar neurons are not lost. Because he did not stain the normally large population of GABAergic neurons in the hilus, it is not known whether a significant change occurred in that population after stimulation of the perforant path. It is possible that such a change did occur, especially in light of the numerous degenerating hilar neurons on the stimulated side. Thus Sloviter's first conclusion, that the GABA-containing hilar neurons are impervious to the stimulation, could be incorrect. Since GABA and somatostatin are colocalized in many hilar neurons in the rat and cat (*3*), Sloviter's second and final conclusions also could be incorrect because the population of somatostatin-containing neurons that appears to be lost in this study would include many GABAergic neurons. Therefore, the proposed novel epilepsy hypothesis, which states that the loss of GABAergic neuron activation by hilar neurons on the stimulated side is the basis for the physiological loss of inhibition, is questionable.

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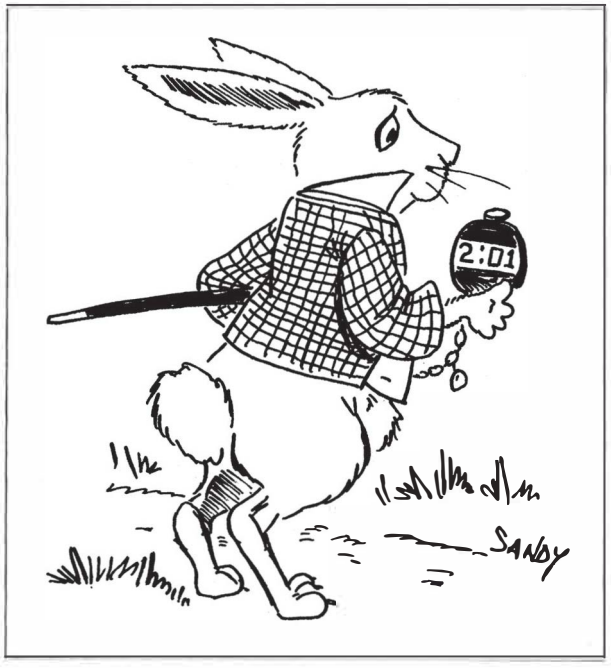
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